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Review

# Ventriculoventricular delay optimization of a cardiac resynchronization device

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ABSTRACT

Cardiac resynchronization therapy (CRT) has become a standard option for patients with severe low cardiac function and mild to severe heart failure. However, its potential has not been maximized to date, as the optimal atrioventricular delay, ventriculoventricular (VV) delay, and tachy therapy settings remain unknown. Here, data from various studies have been used to estimate several CRT settings.

Three search words—interventricular interval, VV delay, and interventricular delay with cardiac resynchronization therapy—were entered into PubMed. The methods used to optimize VV delay included ultrasonography, radioisotope diagnosis, scintigraphy, electrocardiography, Swan–Ganz catheterization, and thoracic impedance. Their populations and results were analyzed to identify convincing rules. Methods for VV delay optimization in the literature can be categorized into four patterns. Time and cost were high in several categories. Most studies concluded that their method was effective but no small amount of papers denied individual detailed optimization. There were some population biases in most papers. Individual optimization had a major impact in patients with ischemic heart disease but no significant impact in patients with non-ischemic heart diseases.

In summary, CRT is an established therapy, but a well-controlled study is required to find conclusive methods for VV delay optimization.



**Contents**



## 1. Introduction

Heart failure is a very common life-threatening disease that incurs a high cost. Therapy for heart failure is important because it not only improves patients' quality of life and prognosis but may also prevent subsequent hospitalization and reduce social medical costs. Optimal therapy for heart failure is needed from both the social and individual perspectives.

### 1.1. Cardiac resynchronization therapy (CRT)

CRT is firmly established but has many areas in need of improvement [1–12]. Particularly, the prognostic value to predict who responds to CRT is not well established [13–19]. Only QRS duration has a confirmed value, the sensitivity of which is insufficient, however [20–22]. The cost of CRT, although more economically reasonable than other therapies, is high; hence, a more effective method to predict responders needs to be established.

In addition, the ideal CRT optimization method is unknown [23]. There are several effective methods, but one has yet to be

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identified as the best [24–28]. Especially regarding VV delay, there are many conflicting methods and theories [29–31].

### 1.2. Categorization of VV delay optimization methods

Methods to optimize VV delay remain competitive; therefore, four categories were created in which to summarize them. The first category focuses on wall motion and dyssynchrony using ultrasonography, scintigraphy, and other techniques [2,3,32–48]. The second category focuses on conduction delays and disorders using electrocardiography and a calculation of lead-to-lead conduction delay time (time between right ventricular pacing and left ventricular sensing and between left ventricular pacing and right ventricular sensing), an electroanatomic mapping system, and other techniques [22,49–63]. The third category considers cardiac output estimated by Swan–Ganz catheterization, thoracic impedance, ultrasonography, and other techniques [55,57,58,64–70]. The fourth category eliminates individual optimization and uses a standard value because these methods acknowledge no major differences in VV delay settings [3,35,71–82].

Since CRT is pacing therapy, it may correct conduction delays but does not improve muscle function. Accordingly, the second category was most appropriate, but most major methods use ultrasonography and a majority of papers in this area claim method efficacy. This may be why we did not want to improve conduction delays; rather, our aim was to relieve heart failure symptoms by increasing cardiac output. The third category matched this aim but in many cases required extensive time and cost. And we decide optimal settings at rest, which may not be optimal during activity time. We do not know whether optimal settings at rest improve a patient's activity and prognosis or not. The fourth category solves this problem: if optimization is not required, it may be the best option.

The first step of this systematic review was determining the need for optimization, followed by identifying the best method to optimize the VV delay.

## 2. Methods and results

A literature search using the PubMed/Medline databases and consensus documents was performed. Searches using “interventricular interval” found 43 studies, “VV delay” found 59 studies, and “interventricular delay” found 200 studies of CRT.

In each study, optimization need, associated methods, optimization modality, and populations were counted. Whenever possible, optimization need as well as method and modality superiority was decided objectively (e.g., the measurement of velocity time integral was not better than the measurement of QRS duration).

A total of 33 studies confirmed the need for optimization and clearly described the superiority of a detailed optimization. These studies used the velocity time integral measured by ultrasonography, the spectrum of wall motion, dyssynchronicity, nuclear imaging, electrocardiography, and other methods. Their superiority was proven by both the instant outcome and the clinical results.

Five studies denied the need for optimization. The nominal settings, including a fixed VV delay (LV > RV of 40 ms or LV = RV), met the clinical purpose. They tended not to measure small details, perhaps since optimal settings change in different situations and small details are of little consequence. If the clinical output is unchanged, there is no need to optimize the VV delay.

Seven studies partially affirmed the need for optimization by removing a detailed check and programing the calculations using pre-populated generator programing (e.g., Quick Opt, St. Jude Medical, Inc.)

The use of ultrasonographic cardiography, the most common modality, for optimization was recommended by 25 studies. The estimation of cardiac output using velocity time integral measurements was most common. Conduction disorders and ventricular muscle dyssynchrony were also improved by spectral measurements, septal wall motion delays, and other techniques.

Ten studies emphasized the importance of conduction delays and stated that electrocardiography was a superior method. In fact, the smallest QRS duration was determined using electrocardiography. There is clear evidence that a wide QRS complex is a prognostic factor of CRT, but it is not clear whether a narrow QRS pacing is preferable.

Seven studies stated that the use of pre-populated programing is both necessary and sufficient. Clinically speaking, it met the demand, but it was unable to obtain the best settings. Therefore, its use might be sufficient for clinical situations.

The ability to obtain a detailed understanding of cardiac function using Swan–Ganz catheterization, thoracic impedance, and other methods has been proven, but few studies have proven their superiority; rather, they stated that cardiac output was changed by VV delay but did not determine its influence on clinical output [65,68].

The populations of these studies had various biases. Despite relatively slight differences in age, sex, and QRS duration, in some studies, > 80% of patients had ischemic heart disease, whereas in others, > 70% of patients had non-ischemic heart disease.

The majority of these studies concluded that their particular method was effective, but most denied that their method was individual, detailed, and had universal optimization. In most studies, the population tended to be weighted in one direction. Individual optimization had some impact in patients with ischemic heart disease but no major impact in patients with non-ischemic heart disease.

In the present study, the effect of population bias was particularly considered. A number of papers that argued that a detailed VV delay optimization improves heart failure contained a large proportion of patients with ischemic heart disease. On the other hand, many papers that claimed that detailed optimization was not important contained a large proportion of patients with non-ischemic heart disease. Hence, it is possible that a detailed VV delay optimization was effective in patients with ischemic heart disease and not needed in patients with non-ischemic heart disease.

CRT is a therapy for conduction disorders. Damaged cardiomyocytes are localized in ischemic heart disease; therefore, in a way, the presence of a conduction disorder is localized and varies among the cases. On the other hand, conduction disorders were not always unequal in patients with non-ischemic heart disease. Localized and inhomogeneous conduction disorders require individualized conduction therapy with CRT, whereas diffuse conduction disorders require only standard settings.

## 3. Conclusion

CRT is a firmly established therapy, but we do not yet know how to maximize its potential at minimum cost. CRT is a costly therapy; hence, its potential should be fully utilized. We should also determine routine CRT settings because its use is becoming more common and an increasing number of CRT devices will be implanted in the future.

Here, VV delay settings, which are very common but controversial, were particularly noted. Upon examining the study findings, a therapy for conduction disorder indicated from the conduction perspective may be decided by conduction delay dispersion.

Conduction disorders were localized and inhomogeneous in patients with ischemic heart disease, in whom CRT efficacy was slightly low; therefore, detailed optimization using echocardiography,

radioisotopes, Swan–Ganz catheterization, and other methods should be carefully performed as needed [83,84].

Dilated cardiomyopathy (DCM) has a relatively homogeneous diffuse conduction order. Clinically simultaneous biventricular pacing was the most common setting for DCM patients. In the future, we can determine the indication for optimization according to specific diseases or heart conditions.

Here, methods for interventricular delay optimization were categorized into four groups. The first category emphasized wall motion and dyssynchrony and used ultrasonography. If dyssynchrony was judged to be high, VV delay optimization using ultrasonography was needed. The second focused heavily on conduction delays and disorders using electrocardiography. If the QRS duration was very wide or had a left bundle branch block pattern, VV delay optimization was needed. Signal-averaged electrocardiography was also useful, but the meaning of its results was uncertain [85]. The third category placed great weight on cardiac output. In patients with very low cardiac output, conduction disorders tended to be high and diffuse and not require optimization. Similarly, in the fourth category, heart disease in which a diffuse conduction disorder was implied did not require optimization. In any case, the need for VV delay optimization might be judged according to a specific disease or conduction disorder pattern; hence, the most effective and least costly settings should be identified.

## Conflict of interest

There is no conflict of interest.

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